

Early intervention can improve outcomes in acute kidney injury

Larmour KE, Maxwell AP. Early intervention can improve outcomes in acute kidney injury.

Practitioner 2015;259(1783):25-28

Dr Kathryn E Larmour
MB BCh MRCP
Specialist Trainee in Renal Medicine

Professor Alexander P Maxwell
MD PhD FRCP
Consultant Nephrologist

Regional Nephrology Unit, Belfast City Hospital, Belfast, UK



Practitioner
Medical Publishing Ltd

Early intervention can improve outcomes in acute kidney injury

AUTHORS

Dr Kathryn E Larmour
MBBCh MRCP
Specialist Trainee in Renal Medicine

Professor Alexander P Maxwell
MD PhD FRCP
Consultant Nephrologist

Regional Nephrology Unit,
Belfast City Hospital,
Belfast, UK

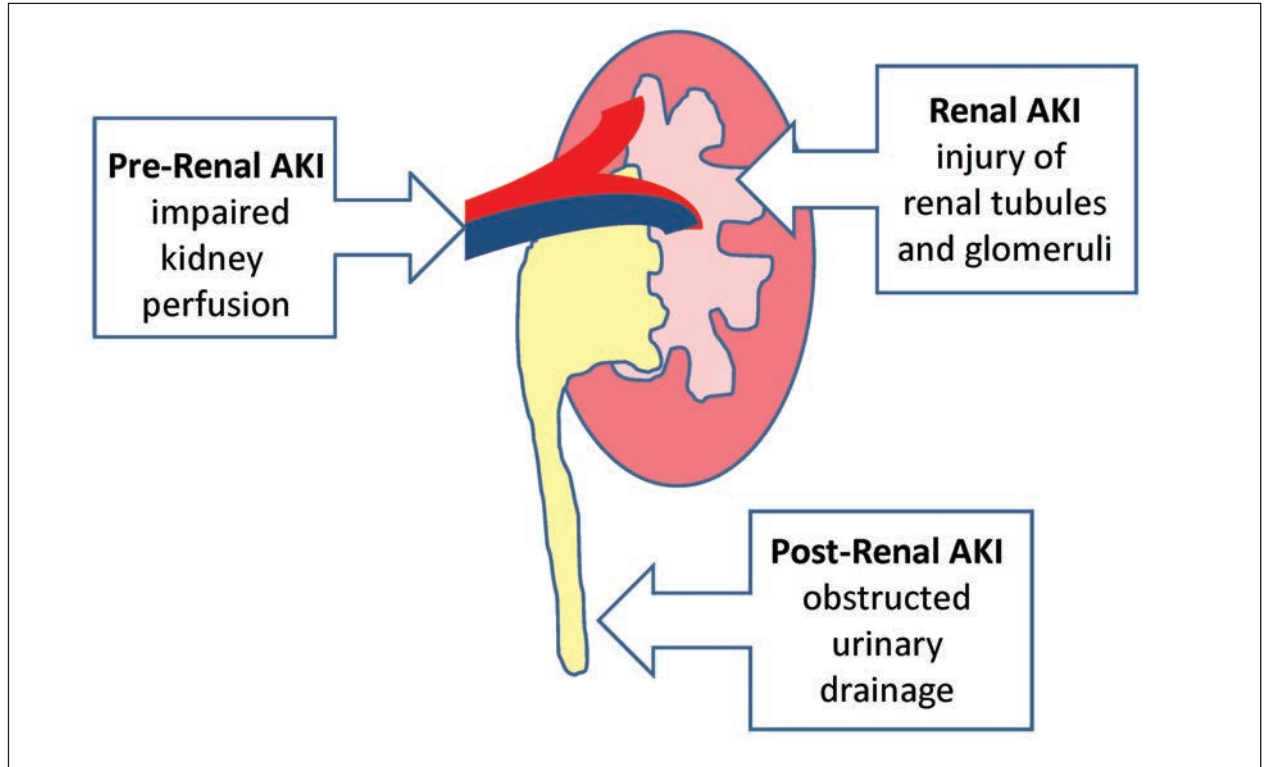


FIGURE 1
Mechanisms contributing to acute kidney injury

What are the causes of acute kidney injury?

How should patients be investigated?

What are the management approaches?



ACUTE KIDNEY INJURY (AKI) IS COMMON, COSTLY TO MANAGE AND ASSOCIATED WITH HIGH MORTALITY.^{1–3}

AKI can occur either in the community or in hospitalised patients and may be challenging to recognise because it is typically asymptomatic.^{1–4}

Opportunities for prevention of AKI are frequently missed and in the absence of symptoms or signs there is often a delay in recognition of established AKI.^{1–4}

Approximately two thirds of hospitalised patients admitted with AKI have developed AKI in the community.^{2,4}

AKI in hospitalised patients is associated with a substantial mortality rate > 20%.^{2,4,5} AKI is a potentially reversible process so improvements in recognition and early interventions could have a major

impact on patient outcomes.

The annual incidence of AKI is rising reflecting an increasingly elderly at-risk population,^{6,7} with multiple comorbidities, coupled with improved detection of AKI following introduction of clinical chemistry laboratory algorithms.^{5,8}

‘Acute kidney injury is potentially reversible’

PRESENTATION

AKI occurs when there is a rapid decrease in glomerular filtration rate (GFR) within hours to days. The loss of kidney function results in the retention

of urea and creatinine and subsequent dysregulation of electrolytes and fluid balance. AKI may occur in individuals with previously normal kidney function or in patients with pre-existing chronic kidney disease (CKD).

Within the community AKI is generally recognised incidentally in the setting of other illness when a U&E test has been ordered and a rise in serum creatinine from baseline is identified.

Although reduction in urine output is a sensitive indicator of renal dysfunction it is unlikely to be noted outside a hospital environment. Most clinical chemistry laboratories now issue electronic alerts (e-alerts), which flag changes in serum creatinine indicative of AKI, helping to identify patients at an earlier stage.^{5,8}

Various factors can increase an



SPECIAL REPORT

ACUTE KIDNEY INJURY

Box 1

Risk factors for acute kidney injury

- Pre-existing CKD (eGFR < 60 ml/min/1.73m²)
- Older age (> 65 years old)
- Sepsis
- Co-existing chronic illness including: cardiac failure, liver disease and diabetes mellitus
- Use of NSAIDs
- Use of ACEi or ARBs and other antihypertensive drugs particularly in the setting of hypovolaemia
- Hypotension (systolic blood pressure < 110 mmHg)
- Symptoms and signs of hypovolaemia
- Urinary tract symptoms
- Previous episode of AKI

individual's susceptibility to AKI and earlier recognition of those at higher risk of AKI is helpful (see box 1, above). Individuals in the community with pre-existing CKD and/or patients treated with an ACE inhibitor (ACEi) or angiotensin receptor blocker (ARB) are at increased risk of AKI if they develop an illness associated with hypovolaemia or hypotension.

The risk of community-acquired AKI is also higher in patients predisposed by other chronic conditions such as heart failure, diabetes or urinary tract obstruction.

Older people have a greater risk of AKI⁷ as they typically have a much lower baseline GFR (natural age-related nephron loss) and may in certain circumstances have limited access to oral fluids.

'AKI may occur in those with previously normal kidney function or pre-existing CKD'

COMMON UNDERLYING CAUSES

Normal kidney function depends on having sufficient arterial perfusion to intact nephrons with adequate urinary drainage. If there is a problem with any of these aspects of kidney function then AKI may occur; see figure 1, p25. The common physiological classification of AKI reflects these three components, see box 2, right.

Pre-renal AKI is very common within the community and may be reversed with restoration of appropriate fluid volume status. Prolonged pre-renal AKI insults may result in acute tubular

necrosis (ATN) which is not 'fluid volume responsive'. Recovery from ATN may be prolonged and the patient's kidney function may not recover to the previous baseline kidney function. AKI caused by acute glomerular disease is much less common within the community.

Following consideration of obvious causes, a less common aetiology for AKI should be considered if clinical features such as fever, rash, joint pains or pulmonary infiltrates are present. Proteinuria and/or haematuria on urinalysis may also indicate a less common cause of AKI.

Thrombocytopenia and haemolytic anaemia with AKI is suggestive of haemolytic uraemic syndrome.

CONFIRMING DIAGNOSIS

Once an unexplained raised serum creatinine is identified this should trigger a careful review of the patient's history including the common AKI risk factors (see box 1, above), medication record, baseline renal function (where known), and clinical examination.

The severity of the AKI should be considered by evaluating the extent of rise of serum creatinine from baseline. Monitoring of GFR is less useful during episodes of AKI as renal function is not in a steady state i.e. the GFR will not be accurate. Patients who have advanced CKD will be more susceptible to complications of AKI since they already have limited renal function.

Potential clues in the history for AKI include reduced fluid intake and/or

increased fluid losses, urinary tract symptoms and recent drug ingestion. AKI secondary to a systemic disease may be associated with other clinical features such as fever, rash, joint pains and non-specific malaise.

'E-alerts flag changes in serum creatinine indicative of AKI'

Clinical examination includes assessment of fluid volume status, which is guided by clinical signs including temperature, peripheral perfusion, heart rate, blood pressure and jugular venous pressure.

Onward referral to hospital should be arranged in the setting of severe hypotension associated with sepsis or fluid losses. Postural changes in pulse and blood pressure are more sensitive indicators of hypovolaemia than supine observations.

The abdomen can be examined carefully for the presence of a palpable bladder. If the history and examination are suggestive of urinary tract obstruction the patient should be referred for urgent ultrasound of renal tracts and discussed with urology services.

Reagent strip urinalysis should be performed, if possible, on any patient with suspected AKI. Positive protein and blood indicators of 2+ to 4+ on urinalysis suggest intrinsic glomerular

Box 2

Classification of acute kidney injury

Classification	Common causes
Pre-renal AKI	Hypotension
	● sepsis
	● medications
	● cardiac failure
Abnormal perfusion to a structurally normal kidney	Hypovolaemia
	● vomiting and diarrhoea
	● dehydration
	● blood loss
	Hypoxia
Renal AKI	Prolonged pre-renal AKI insults
	Acute tubular necrosis (ATN)
Injury to nephrons (glomeruli and tubules)	Drugs/toxins
	Glomerulonephritis
	Interstitial nephritis
	Vasculitis
Post-renal AKI	Obstruction
	● ureteric stones
Obstruction to urinary flow	● pelvic malignancy
	● prostate hypertrophy

disease and should trigger more urgent referral to hospital. A high specific gravity (> 1.020) suggests fluid volume depletion and increased oral fluid intake may be appropriate.

The laboratory investigations for AKI may include:

- U&E (with particular reference to concentrations of urea, creatinine, sodium, potassium and bicarbonate)
- Full blood count
- CRP
- Liver function tests
- Glucose
- Bone profile
- Immunological tests for rarer causes of AKI include:

— anti-neutrophil cytoplasmic antibodies (for vasculitis)

— anti-glomerular basement membrane antibody (for anti-GBM disease)

— autoantibody screen including anti-dsDNA titre and complement levels (for SLE and lupus nephritis)

— serum free light chains, serum immunoglobulins, plasma protein electrophoresis (for myeloma).

‘Older people have a greater risk of AKI as they have a much lower baseline GFR’

MANAGEMENT

There are no specific pharmacological treatments for AKI. The focus of AKI management is correcting the conditions causing or contributing to it.

Fluid balance

It is critical that the fluid volume status of patients with AKI is accurately assessed through careful history and examination. Increased oral intake should be encouraged in the setting of hypovolaemia or dehydration however inadvertent fluid overload should be avoided. The patient may be encouraged to monitor their weight to aid assessment of their volume status.

Drugs that affect AKI

Stop, at least temporarily, drugs that may induce, exacerbate or complicate AKI. Drugs such as diuretics, ACEi, ARBs, NSAIDs will exacerbate hypoperfusion of kidneys and should be withheld until the patient has recovered and AKI has resolved.

Blood pressure

It is important to restore an effective blood pressure. Septic patients should be referred to hospital for fluid resuscitation and antibiotics.

Infections that may be contributing to hypotension should be treated early.

‘Stop, at least temporarily, drugs that may induce, exacerbate or complicate AKI’

Medication review

Medications commonly contribute to the development of AKI. In addition, because of a sudden reduction in kidney function associated with AKI, many drugs require dose reduction to avoid hazardous side effects. All regular medications should be reviewed, see table 1, right.

Careful monitoring of potassium is required if initiating medications that might aggravate hyperkalaemia in patients with advanced CKD who are already at risk.

REFERRAL TO NEPHROLOGY

It is not necessary to refer all patients with AKI to hospital if they are responding to timely community management of their underlying medical condition.

Early contact with a nephrology team is advised for those patients who may require dialysis or for whom intrinsic renal disease is considered to be the most likely cause of their AKI.

Outpatient referral to a nephrologist

can be considered for individuals who appear to have recovered from their AKI but have a persisting eGFR < 30 ml/min/1.73m² or significant proteinuria (urinary albumin/creatinine ratio > 50 mg/mmol). If a patient is already under review by a nephrology team it would be helpful to inform the nephrologist if AKI occurs in patients with CKD stage 4 or 5 or in renal transplant recipients.

It is also possible that AKI may be >>

Table 1

Drugs that complicate management of acute kidney injury

Drugs interfering with renal perfusion

ACEi and ARBs
NSAIDs
All antihypertensives
Diuretics
Nitrates
Nicorandil

Drugs requiring dose reduction or cessation

Low molecular weight heparins
Opiates
Penicillin-based antibiotics
Metformin
Sulfonylurea-based hypoglycaemic agents
Aciclovir

Drugs requiring close monitoring

Warfarin

Drugs aggravating hyperkalaemia
Digoxin
Beta-blockers
Trimethoprim
Potassium-sparing diuretics e.g. eplerenone, spironolactone, amiloride

Box 3

Medicine sick day rules that may reduce the risk of acute kidney injury

When you are unwell with any of the following:

- Vomiting or diarrhoea
- Fevers, sweats or shaking

Then stop the drugs listed below.

Medications to stop

- ACE inhibitors: names ending in ‘pril’
- ARBs: names ending in ‘sartan’
- NSAIDs: anti-inflammatory painkillers; e.g. ibuprofen, diclofenac, naproxen
- Diuretics: ‘water tablets’ e.g. furosemide, spironolactone, indapamide, bendroflumethiazide
- Metformin

Restart when you are well (after 24-48 hours eating and drinking normally)

key points

SELECTED BY

Dr Peter Saul

GP, Wrexham and Associate GP Dean for North Wales

The incidence of acute kidney injury (AKI) is rising

reflecting an increasingly elderly at-risk population, with multiple comorbidities, coupled with improved detection of AKI following introduction of clinical chemistry laboratory algorithms. AKI is a potentially reversible process so improvements in its recognition and early interventions could have a major impact on patient outcomes.

AKI occurs when there is a rapid decrease in GFR

within hours to days. The loss of kidney function results in the retention of urea and creatinine and subsequent dysregulation of electrolytes and fluid balance. Individuals in the community with pre-existing CKD and/or patients treated with an ACE inhibitor (ACEi) or angiotensin receptor blocker (ARB) are at increased risk of AKI if they develop an illness associated with hypovolaemia or hypotension.

Pre-renal AKI is very common within the community and

may be reversed with restoration of appropriate fluid volume status. Potential clues in the history for AKI include reduced fluid intake and/or increased fluid losses, urinary tract symptoms and recent drug ingestion. Postural changes in pulse and blood pressure are more sensitive indicators of hypovolaemia than supine observations.

Once an unexplained raised serum creatinine is identified

this should trigger a careful review of the patient's history including the common AKI risk factors, medication record, baseline renal function (where known) and clinical examination. The severity of the AKI should be considered by evaluating the extent of rise of serum creatinine from baseline.

Reagent strip urinalysis should be performed,

if possible, on any patient with suspected AKI. Positive protein and blood indicators of 2+ to 4+ on urinalysis suggest intrinsic glomerular disease and should trigger more urgent referral to hospital.

The focus of AKI management is correcting the conditions

causing or contributing to it. It is critical that the fluid volume status of patients with AKI is accurately assessed through careful history and examination. Drugs that may induce, exacerbate or complicate AKI such as diuretics, ACEi, ARBs, NSAIDs should be stopped. It is important to restore an effective blood pressure.

It is not necessary to refer all AKI patients to hospital

if they are responding to timely community management of their underlying medical condition. Individuals at increased risk of AKI, and their main carers, can be educated about sick day rules i.e. temporary cessation of certain drugs (diuretics, ACEi, ARBs, metformin, NSAIDs) during episodes of acute illness. Advice cards with sick day rules and medications to be stopped can be given to patients.

part of a terminal illness reflecting progression of an advanced untreatable comorbidity. In this setting the appropriateness of onward referral to hospital or a nephrology clinic can be reconsidered.

IMPROVING OUTCOMES

The majority of episodes of AKI occur within the community and GPs play a vital role in the early identification and management of individuals with AKI.⁹

Ideally, renal function should be monitored during any episodes of acute illness associated with sepsis, volume depletion or hypotension.

A careful review of prescribed medications is always appropriate with the aim of stopping any potentially nephrotoxic drugs.

Individuals at increased risk of AKI (and their main carers) can be educated about sick day rules i.e. temporary cessation of certain drugs (diuretics, ACEi, ARBs, metformin, NSAIDs) during episodes of acute illness. Advice cards with sick day rules and medications to be stopped can be given to patients, see box 3, p27.¹⁰

'Careful prescribing is a key component in reducing future risk of AKI'

Prescribing decisions can have a significant impact on the risk of community AKI. Co-prescription of NSAIDs with an ACEi or ARB is a potentially nephrotoxic combination. Temporarily withholding these medications in acute illness, e.g. vomiting and diarrhoea, can help to reduce the risk of AKI. The risk of ongoing prescription of potential nephrotoxic medications should be considered if the patient will be at continued risk of hypovolaemia.

CONCLUSION

AKI is a common, costly and potentially reversible condition, associated with high mortality.

Identifying and educating individuals at high risk of AKI, particularly about the potential harm of co-prescribed medications, may limit the severity of AKI. Careful prescribing within the community is a key component in reducing future risk of AKI. GPs play a central role in the early identification and management of patients with AKI.

Timely liaison between primary and secondary care and ease of access to services is required to lessen the impact of AKI on patients in the community.

REFERENCES

- 1 Stewart J, Findlay G, Smith N et al. Adding insult to injury. A review of the care of patients who died in hospital with a primary diagnosis of acute kidney injury. National Confidential Enquiry into Patient Outcome and Death. NCEPOD. London. 2009 www.ncepod.org.uk/2009report/Downloads/AKI_report.pdf
- 2 Kerr M, Bedford M, Matthews B, O'Donoghue D. The economic impact of acute kidney injury in England. *Nephrol Dial Transplant* 2014;29(7):1362-8
- 3 Chertow GM, Burdick E, Honour M et al. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. *J Am Soc Nephrol* 2005;16(11):3365-70
- 4 Wonnacott A, Meran S, Amphlett B et al. Epidemiology and outcomes in community-acquired versus hospital-acquired AKI. *Clin J Am Soc Nephrol* 2014;9(6):1007-14
- 5 Selby NM, Crowley L, Fluck RJ et al. Use of electronic results reporting to diagnose and monitor AKI in hospitalized patients. *Clin J Am Soc Nephrol* 2012;7(4):533-40
- 6 Susantitaphong P, Cruz DN, Cerda J et al. Acute Kidney Injury Advisory Group of the American Society of Nephrology. World incidence of AKI: a meta-analysis. *Clin J Am Soc Nephrol* 2013;8(9):1482-93
- 7 Coca SG. Acute kidney injury in elderly persons. *Am J Kidney Dis* 2010;56(1):122-31
- 8 Porter CJ, Juurlink I, Bisset LH et al. A real-time electronic alert to improve detection of acute kidney injury in a large teaching hospital. *Nephrol Dial Transplant* 2014;29(10):1888-93
- 9 Blakeman T, Harding S, O'Donoghue D. Acute kidney injury in the community: why primary care has an important role. *Br J Gen Pract* 2013;63(609):173-4
- 10 Morrison C, Wilson M. Medicine sick day rules cards - interim evaluation. NHS Highland <http://margaretmccartney.com/wp-content/uploads/2014/10/NHS-interim-evaluation-medicine-sick-day-rules.pdf>

Useful information

Think kidneys

www.thinkkidneys.nhs.uk

NICE CG169

Acute kidney injury. Prevention, detection and management of acute kidney injury up to the point of renal replacement therapy www.nice.org.uk

GAIN

Guidelines and Audit Implementation Network. Northern Ireland guidelines for acute kidney injury www.gain-ni.org/images/GAIN_-_AKI_-_Northern_Ireland_Guidelines_for_Acute_Kidney_Injury_PDF.PDF

We welcome your feedback

If you would like to comment on this article or have a question for the authors write to: editor@thepractitioner.co.uk